WHAT IS CLAIMED IS:

1.   A method for identifying an agent that alters processing of a
membrane protein of interest, comprising:

contacting the agent with an animal host cell that expresses the membrane
protein and at least one processing enzyme of the membrane protein, and

5   detecting altered processing of the membrane protein to identify the agent
that alters the processing of the membrane protein

2.   The method of claim 1, wherein detecting the altered membrane
protein processing comprises assessing the relative presence or absence of at least one
10 species of membrane protein fragment on the surface of the host cell or released from the
surface of the host cell.

3.   The method of claim 2, wherein the at least one species of
membrane protein fragment is released from the surface of the host cell.

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4.   The method of claim 1, wherein the at least one membrane protein
processing enzyme is a protease or a phospholipase.

5.   The method of claim 1, wherein the altered membrane protein
20 processing results in a decreased production of a fragment of the membrane protein
released from the cell surface.

6.   The method of claim 5, wherein the released fragment is associated
with an increased risk of disease.

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7.   The method of claim 6, wherein the disease is an inflammatory
disease, cancer, diabetes, Alzheimer's disease, or Parkinson's disease.

8.   The method of claim 1, wherein the agent is from a compound
30 library.

9.   The method of claim 8, wherein the compound library is a combinatorial chemical library.

10.   The method of claim 8, wherein the compound library is a natural products library.

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11.   The method of claim 8, wherein the compound library is a peptide library.

12.   The method of claim 1, wherein the agent is a small molecule.

13.   The method of claim 1, wherein the agent is a biomolecule.

14.   The method of claim 13, wherein the biomolecule is a peptide.

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15.   The method of claim 14, wherein the peptide is produced by transcription and translation from an oligonucleotide encoding the peptide.

16.   The method of claim 15, wherein the oligonucleotide has a length of about 18 to about 120 nucleotides.

17.   The method of claim 15, wherein the oligonucleotide has a length of

15   about 36 to about 60 nucleotides.

18.   The method of claim 15, wherein contacting the peptide with the host cell comprises introducing an expression vector, the expression vector comprising the oligonucleotide encoding the peptide, into the host cell, the host cell thereby expressing and displaying the peptide within a secretory pathway and on an extracellular cell surface.

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19.   The method of claim 15, wherein the oligonucleotide is from an expression library comprising a plurality of oligonucleotides, at least of majority of the oligonucleotides having different sequences encoding a different peptide.

20.   The method of claim 19, wherein the sequence of the plurality of oligonucleotides is randomized.

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21.   The method of claim 19, wherein the expression library is pre-

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enriched for oligonucleotides encoding peptides that specifically bind to the membrane protein.

22.   The method of claim 19, wherein the contacting of the peptide with the host cell comprises introducing the expression library into a first plurality of animal

5   host cells that express the membrane protein and at least one processing enzyme of the membrane protein, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface.

23.   The method of claim 22, further comprising:

selecting from the first plurality of host cells displaying the different

10   peptides a first subset of host cells that exhibit altered membrane protein processing; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of the membrane protein.

24.   The method of claim 22, wherein the first plurality of host cells

15   displaying the different peptides have been enriched using a selectable marker.

25.   The method of claim 24, wherein the selectable marker is V5, FLAG, or thioredoxin.

26.   The method of claim 24, wherein the enrichment comprises magnetic bead selection.

20   27.   The method of claim 24, wherein the enrichment comprises selection by fluorescence-activated cell sorting.

28.   The method of claim 24, wherein the host cells expressing and displaying the different peptides on the extracellular cell surface express a high copy number of the different peptides.

25   29.   The method of claim 15, wherein the peptide is displayed as a fusion protein with a presentation molecule.

30.   The method of claim 29, wherein the presentation molecule is CD24.

31.   The method of claim 29, wherein the presentation molecule is IL-3 receptor.

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32.   The method of claim 29, wherein the presentation molecule is thioredoxin.

33.   The method of claim 29, wherein the fusion protein further comprises a marker epitope.

34.   The method of claim 33, wherein the marker epitope is

10   polyhistidine, V5, FLAG, or myc

35.   The method of claim 29, wherein the fusion protein further includes a signal for a glycophosphatidylinositol (GPI) anchorage.

36.   The method of claim 1, wherein the animal host cell is a mammalian host cell.

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37.   The method of claim 1, wherein the animal host cell is a recombinant host cell.

38.   The method of claim 37, wherein the animal host cell is an isolated cell.

39.   The method of claim 1, wherein the agent is contacted with the host

20   cell under substantially physiological conditions.

40.   The method of claim 39, wherein the substantially physiological conditions comprise the presence of a complex biological fluid.

41.   The method of claim 40, wherein the complex biological fluid is blood, serum, plasma, or cerebral spinal fluid (CSF).

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42.   The method of claim 2, wherein the assessment of the relative

presence or absence of at least one species of a membrane protein fragment on the cell surface comprises contacting the host cell with at least one detectably labeled marker that specifically binds to the at least one species of membrane fragment and detecting the bound, labeled marker.

5   43.   The method of claim 42, wherein the at least one marker is an antibody that binds to a predetermined epitope of the membrane protein or a membrane protein fragment.

         44.   The method of claim 43, wherein the assessment of the relative presence or absence of at least one species of membrane protein fragment on the cell

10   surface further comprises determining a ratio of the detection signals of at least two labeled antibodies specific for at least two different epitopes of the membrane protein or a membrane protein fragment.

         45.   The method of claim 1, wherein the agent is an allosteric effector of the membrane protein.

15   46.   The method of claim 1, wherein the detecting altered processing of the membrane protein on the surface of the host cell comprises the use of a flow sorter.

         47.   A method for identifying a peptide that alters processing of an angiotensin converting enzyme (ACE) membrane protein comprising:

                 introducing an expression library comprising a plurality of

20   oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express ACE membrane protein and at least one ACE processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface;

25   selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered ACE processing; and

                 identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that

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alters the processing of ACE.

48.   The method of claim 47, wherein the animal host cell is a mammalian host cell.

49.   The method of claim 47, wherein the animal host cell is a
5   recombinant host cell.

50.   The method of claim 47, wherein the animal host cell is an isolated cell.

51.   The method of claim 47, wherein the first plurality of host cells display the different peptides under substantially physiological conditions.

10   52.   A method for identifying a peptide that alters processing of ACE membrane protein comprising:
    pre-enriching an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, for at least one oligonucleotide that encodes a peptide that
15   specifically binds to ACE, the pre-enrichment comprising the steps of
    introducing the expression library into a phage display vector which can express the peptides encoded by the oligonucleotide sequences on the surface of the phage;
    expressing the different peptides on the surface of the phage;
20   selecting a subset of phage particles that express peptides that specifically bind ACE membrane protein;

    recovering the oligonucleotide sequences from the selected phage particles to form a pre-enriched expression library

25   introducing the pre-enriched expression library into a first plurality of animal host cells that express ACE membrane protein and at least one ACE membrane protein processing enzyme, the host cells thereby expressing and displaying the at least one ACE-binding peptide within a secretory pathway and on an extracellular cell surface;

selecting from the first plurality of host cells displaying the at least one ACE membrane protein-binding peptide a first subset of host cells that exhibit altered ACE processing; and

5   identifying from the first subset of host cells a first sub-library of the pre-enriched expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of ACE.

53.   A method for identifying a peptide that alters processing of ACE membrane protein comprising:

introducing an expression library comprising a plurality of
10   oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express ACE membrane protein and at least one ACE membrane protein processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface;

15   selecting from the first plurality of host cells displaying the different peptides a first subset of host cells that exhibit altered ACE processing; wherein the altered ACE processing is determined by assessing the relative presence or absence of at least one species of ACE released from the surface of the host cells displaying the different peptides by contacting the host cells with at least one detectably labeled marker
20   that specifically binds to the at least one species of ACE fragment and detecting the bound labeled marker; and

identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of ACE membrane protein.

25   54.   A method for identifying a peptide that alters processing of ACE membrane protein comprising:

introducing an expression library comprising a plurality of oligonucleotides, at least a majority of the oligonucleotides having different sequences encoding different peptides, into a first plurality of animal host cells that express ACE

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membrane protein and at least one ACE processing enzyme, the host cells thereby expressing and displaying the different peptides within a secretory pathway and on an extracellular cell surface under substantially physiological conditions;

     selecting from the first plurality of host cells displaying the different

5   peptides a first subset of host cells that exhibit altered ACE processing; wherein the altered ACE processing is determined by assessing the relative presence or absence of at least one species of ACE fragment on the surface or released from the surface of the host cells displaying the different peptides by contacting the host cells with at least one detectably labeled marker that specifically binds to the at least one species of ACE

10   fragment and detecting the bound labeled marker; and

     identifying from the first subset of host cells a first sub-library of the expression library comprising at least one oligonucleotide that encodes the peptide that alters the processing of ACE membrane protein.